IN THE TITLE:

Please replace the current title with the following title:

NUCLEIC ACIDS ENCODING INTERLEUKIN-1 INHIBITORS AND PROCESSES FOR PREPARING INTERLEUKIN-1 INHIBITORS

IN THE SPECIFICATION:

Please amend the specification as follows:

Please replace the paragraph beginning on page 17, line 8, with the following paragraph:

Figure 4 depicts the mono S ion exchange chromatography of: Figure 4A; Chromatogram A, the pegylation reaction mixture of $mPEG_{5000}^{*}$ IL-1ra, peak 1 is the modified and peak 2 is the unmodified IL-1ra; and Figure 14B; Chromatogram B, shows the purified $mPEG_{5000}^{*}$ IL 1-ra.

Please replace the paragraph beginning on page 17, line 16, with the following paragraph:

Figure 6 depicts the reverse phase HPLC fractionation of tryptic digest of alkylated $mPEG_{5000}$*IL-1ra reacted with tritiated iodoacetic acid to label free cysteines. Separation was performed on a Brownlee C8 (2.1 x 220mm) column at ambient temperature and a flow rate of 1000 µl/min with a linear gradient. Solvent A was 0.1% TFA in water and solvent B was 0.085% TFA in 80% acetonitrile and 20% H_2O. Figure 6 shows peaks 1 through 18.

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Please replace the paragraph beginning on page 17, line 24, with the following paragraph:

Figure 7 depicts the reverse phase HPLC fractionation of chymotryptic digest of peptide 18 in figure 6. Conditions were identical to those in Figure 6. Peptides 5 and 8 contained tritium counts and peptide 5 had the amino acid sequence LCTAMEADQPVSL. The cysteine was identified as the carboxymethylcysteine derivative. This cycle was the only one containing counts above background. The amino acid sequence of peptide 8 began with serine 103 of IL-1ra. Redigestion of this peptide with chymotrypsin permitted fractionation of all tritium counts from the peptide. Figure 7 shows peaks 1 through 7.

Please replace the paragraph beginning on page 18, line 17, with the following paragraph:

Figure 13 compares IL-6 levels induced in mice by five ratios of c105 30kDa TNF inhibitor to TNF (Figure 13A) and five ratios of c105 30kDa TNF inhibitor to PEG_{2000}db to TNF (Figure 13B).

Please replace the paragraph beginning on page 18, line 24, with the following paragraph:

Figure 15 depicts percent neutrophils induced by varying ratios of TNF to c105 30kDa TNF inhibitor (Figure 15A), c105 30kDa TNF inhibitor PEG_{3500}db (Figure 15B); c105 30kDa TNF inhibitor $PEG_{10,000}$db (Figure 13C); and c105 30kDa TNF inhibitor $PEG_{20,000}$db (Figure 15D).

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Please replace the paragraph beginning on page 42, line 13, with the following paragraph:

The mPEG$_x$*IL-1ra can be purified using a MonoS (Pharmacia) column with 20mM MES buffer at pH 5.5. The proteins were eluted from the column using a salt gradient from 0 to 500mM NaCl in the same buffer. For example, unmodified IL-1ra elutes at 220mM NaCl, while the purity is assessed by various techniques including analytical ion exchange chromatography and SDS-PAGE. mPEG$_{5000}$ IL-ra elutes at 160mM (Figures 4A and 4B).

Please replace the paragraph beginning on page 42, line 32, with the following paragraph:

Purified mPEG$_x$*IL-1ra gave a single symmetrical peak upon rechromatography on MonoS and appeared pure by both SDS-PAGE and size exclusion chromatography (Figure 3 and Figure 4B). A comparison of the tryptic maps of IL-1ra and mPEG$_{5000}$*IL-1ra showed one peak, corresponding to the peptide containing c116 and c122, absent from the conjugate map with the appearance of a new broad peak in this map. Subdigestion of this new peak with chymotrypsin and subsequent amino acid sequence analysis indicated that c116 had been pegylated under the conditions employed (Figure 6).

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Please replace the paragraph beginning on page 54, line 28, with the following paragraph:

The potency of c105 30kDa TNF inhibitor PEG_{2000} dumbbell with that of the unpegylated c105 30kDa TNF inhibitor was compared. Human recombinant TNF was injected intravenously at a dose of 10ug per mouse either alone or simultaneously with the TNF inhibitors. Four different reactions of inhibitors to TNF were tested (Figures 13A and 13B). The ratios were calculated based on protein content. Three mice were tested at each dose. Blood was collected at two hours after the intravenous injections. IL-6 levels were measure by ELISA.

Please replace the paragraph beginning on page 57, line 6, with the following paragraph:

The potency of unpegylated c105 30kDa TNF inhibitor with three pegylated species of c105 30kDA TNF inhibitor ($PEG_{3,500}$, $PEG_{10,000}$ and $PEG_{20,000}$ dumbbells) was also compared. Keeping the TNF stimulus constant at 7.5 ng per mouse, the inhibitors were tested at ratios of 100:1, 10:1, and 1:1 (c105 30kDa TNF inhibitor species: TNF). The ratios were calculated based on protein content. The mice were injected subcutaneously with the c105 30kDa TNF inhibitor simultaneous to the intraperitoneal administration of TNF. Six mice were tested in each dose group. Four hours later the peritoneal lavage fluid was collected and analyzed. Values shown in Figures 15A, 15B, 15C, and 15D are the percentage neutrophils in the peritoneal lavage fluid. The lowest ratio at which the unpegylated c105 30kDa TNF inhibitor and c105 30kDa TNF inhibitor $PEG_{3,500}$ dumbbell significantly inhibited neutrophil migration is 100:1. The c105 30kDa TNF inhibitor $PEG_{10,000}$ and $PEG_{20,000}$ dumbbells significantly inhibited neutrophil migration at a ratio of 10:1.

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